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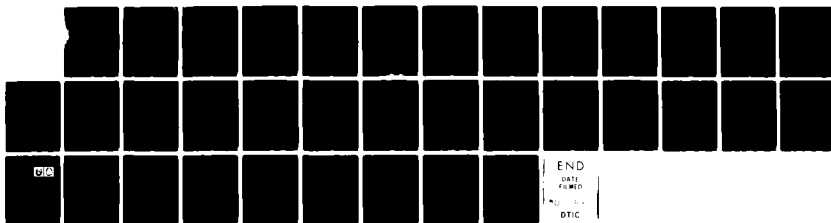
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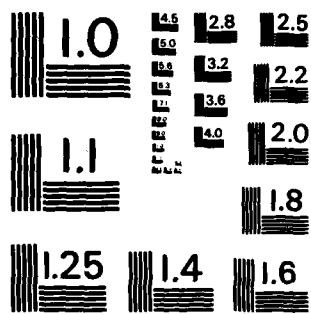
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DEPARTMENT OF PSYCHOLOGY —

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In this chapter, we describe some properties of brain magnetic activity and review the recent application of magnetoencephalography to the study of both normal human brain function and cases of cerebral pathology.

Although little direct evidence exists concerning the cellular mechanisms that generate the magnetoencephalogram, a consideration of the physical properties of central nervous system neurons is instructive. The magnetic fields recorded from the scalp must reflect the activity of local collections of neurons sharing a similar orientation and pattern of discharge. Thus, as in the EEG, the MEG must result from the synchronous activity of populations of anatomically similar neurons.

It is widely believed that synaptic potentials form the basis of

recordable brain magnetic activity. Action potentials, although large in amplitude, produce multiphasic potential changes occurring very fast. Thus, it is difficult for the activity of many neurons to fire in the synchronous manner required to produce a magnetic field observable at the surface of the scalp. However, the slower synaptic activity in the larger central nervous system (CNS) neurons are synchronized more easily. Thus, synaptic potentials, rather than action potentials, are thought to be reflected in MEG recordings.

Central nervous system neurons contribute unequally in generating both EEG and MEG. Although stellate and granular cells are very numerous, their contribution to extracranial magnetic fields is probably minimal due to their small size and randomly oriented dendritic fields. In contrast, populations of similarly oriented pyramidal cells, with their long (up to 4mm; Shepherd, 1979) apical dendrites can generate substantial magnetic fields when simultaneously activated. Groups of parallel pyramidal cells are generally considered to be the most important source of the MEG. At a distance, these cell groups produce an electrical activity that can be approximated by current dipoles. A current dipole is a source having a determined linear orientation and a minimal extent. As has been recognized previously for the EEG (Creutzfeldt, 1974), the magnetic activity of a localized source in the brain is often usefully modeled as a single current dipole or as a local dipole layer (Lopes da Silva & van Rotterdam, 1982).

3.0 BRAIN MAGNETIC FIELDS ARE SPATIALLY RESTRICTED.

Unlike its electrical counterpart, the magnetic field produced by the activation of a local population of CNS neurons is restricted to the region of its origin. There are several reasons for the highly localized distribution of magnetic fields about a dipole current source. First, in an infinite homogeneous conducting volume, only the intracellular flow of current produces a measurable magnetic field; the fields produced by the volume conducted return current flow tend to be self-cancelling (Cohen & Hosaka, 1976). In most simple situations in which the conducting medium has a boundary such as the skull, the magnetic field orthogonal to the boundary is only affected by the intracellular current (Cuffin & Cohen, 1977). Volume currents will however affect the tangential component of the field at the surface.

Second, the magnetic field is highly dependent on the current density of intracellular current flow. In the case of a current dipole, the magnetic field decreases with the square of the distance to the source. However, the EEG is a measure of volume currents that are widely distributed throughout the conducting medium of brain tissue. Thus, the strength of the electrical field does not have the same relationship to distance as does the magnetic field.

Third, the skull is virtually transparent to magnetic fields whereas it behaves as a high resistivity barrier for the electrical field. This high resistance compared to adjacent brain regions results in "smearing" of the

scalp electrical potential (Cooper, Winter, Crow, and Walter, 1965).

Finally, in simple bounded conducting volumes such as spheres, radial sources do not produce an external magnetic field (Baule & McFee, 1965). The magnetic field is selectively sensitive to the component of the source that is tangential to the surface of the volume. Thus, dipoles with the same location but at different tilts in relation to the surface will produce the same magnetic field distribution. However, because the electric field is influenced by both radial and tangential components of the source, its distribution will be very sensitive to the orientation of the dipole (Williamson & Kaufman, 1981a). For a dipole having a large radial component, the pole closest to the surface will generally dominate the electrical field; for this and other reasons dipoles from very different origins may produce very similar electrical field patterns.

Thus, in contrast to the electrical field, the magnetic field is concentrated in the region of the neurons that generate it. The magnetic field of a dipole describes circles around the source which at the scalp are measured as magnetic flux emerging from the head on one side of the source and reentering the head on the other side of the source. The field obeys the "right-hand rule" of elementary physics; for a current source oriented in the direction of the thumb of the right hand, the resulting magnetic field will circulate in the direction of the curled fingers. The electrical field should ideally be of opposite polarities at the two ends of the source. Figure 1 illustrates the orientation of both electrical and magnetic fields about a current dipole. The electrical field rarely has such a simple configuration, whereas the magnetic field recorded from a number of cortical sources is often found to approximate this pattern.

4.0 THE STRENGTH OF BRAIN MAGNETIC FIELDS.

Brain magnetic fields are very weak, particularly compared with typical magnetic disturbances produced by non-biological sources in the environment. This may be seen in Figure 2. Magnetic field strength is best described in terms of flux density (or magnetic induction). The standard unit of flux density in the Systeme International (SI) is the tesla, named for the American engineer and inventor, Nicola Tesla. The tesla is a secondary unit equal to 1 newton/ampere-meter, where a newton is equal to 1 kilogram-meter/second squared.

The flux density of brain magnetic fields is on the order of 0.01-1 picotesla. This is two orders of magnitude smaller than the fields produced by skeletal or cardiac muscle, six orders of magnitude smaller than the fields produced by large moving metal objects such as automobiles and elevators, and eight orders of magnitude smaller than the magnetic field of the earth. These considerations pose two requirements for the measurement of the magnetic fields of the brain: first, the measurement system must be very sensitive and, second, a substantial signal-to-noise ratio problem must be solved.

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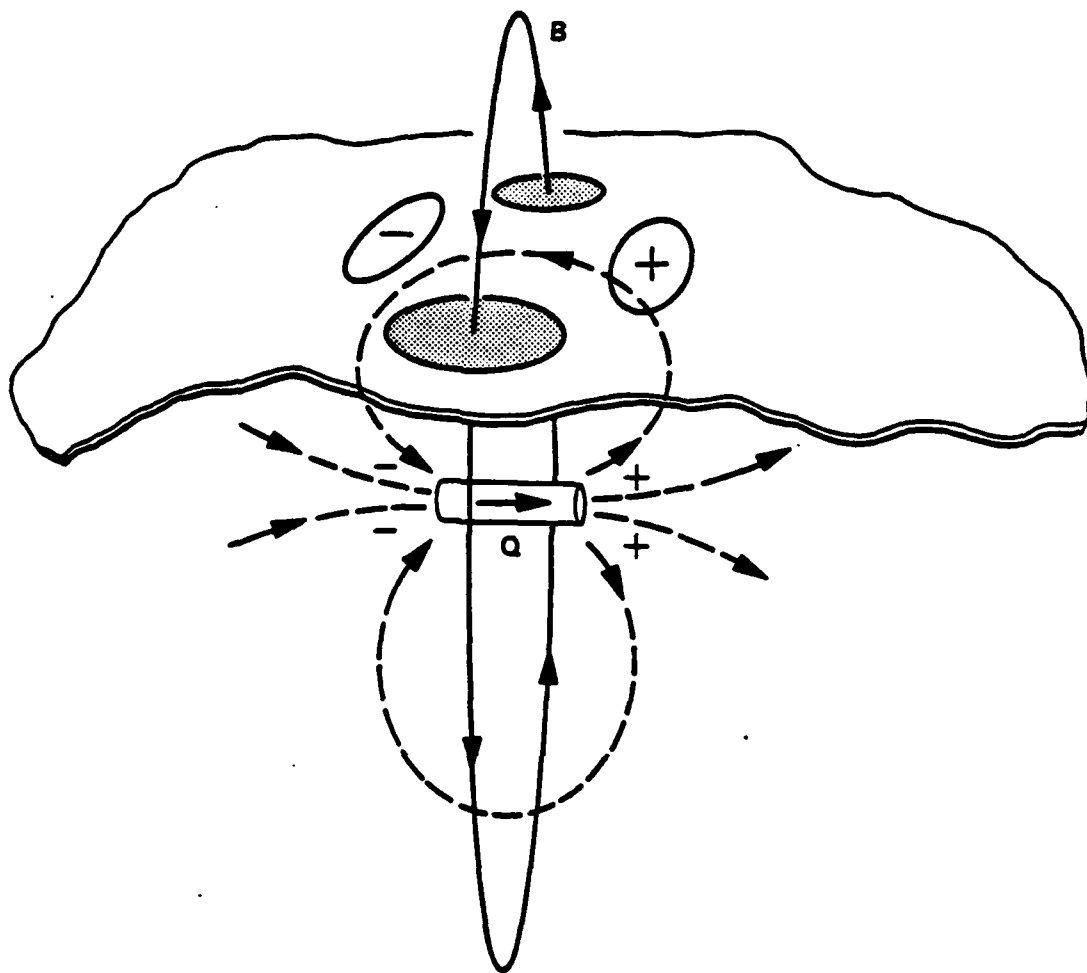


Figure 1. Theoretical distributions of electrical and magnetic fields produced on a surface by a current dipole lying tangentially in a conducting medium below the surface. Dotted lines represent the volume currents producing the surface electrical field. The continuous line is the magnetic field (B) produced by the dipole (Q). (Adapted from Kaufman, Okada, Brenner, & Williamson, 1981).

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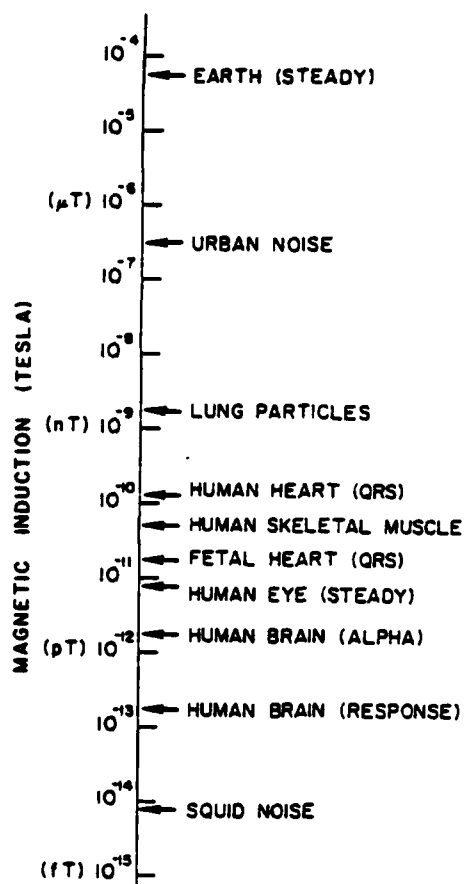


Figure 2. Magnetic induction of sources relevant to biomagnetic measurement. The human brain response level of 120 fT is for some of the strong components of the sensory ERFs. (From Williamson, Kaufman, & Brenner, 1977).

5.0 MEASURING BRAIN MAGNETIC FIELDS.

The problem of measuring the weak magnetic fields produced by biological sources is not trivial. Gengerelli, for example, tried unsuccessfully in 1942 to detect the magnetic field produced by stimulation of the frog's sciatic nerve using a detection coil of 30 turns of wire. However in a second attempt 20 years later, using an improved 12,000 turn coil, Gengerelli was able to measure that magnetic field with success (Gengerelli, 1961). In a similar way, Baule & McFee (1963) recorded the first magnetocardiogram and Cohen (1968) using a magnetically shielded room recorded the first signs of the alpha rhythm in the MEG. However, this straightforward approach to magnetic field measurement was not well suited for the study of the central nervous system.

The reliable measurement of the weak magnetic fields of the central nervous system was made possible by the development of a highly sensitive magnetic sensor called the superconductive quantum interference device (SQUID) developed by Zimmerman and colleagues in 1970 (Zimmerman, 1972; Zimmerman, Thiene, & Harding, 1970). The SQUID may be used to sense magnetic fields directly or be coupled to specially designed superconducting detection coils. Perhaps the simplest configuration for the detection coil is a single loop of wire. Although very sensitive, such a design is incapable of rejecting environmental noise and must therefore be operated in magnetically shielded rooms or in remote locations. The input coils can also be given more complex configurations that would cancel magnetic noise. One that is widely used is that of a second-order gradiometer, a concentric set of coils sensing the second spatial derivative of the field gradient traversing them (Baule & McFee, 1965; Brenner, Williamson, Kaufman, 1975). This configuration makes the gradiometer selectively sensitive to very close sources relative to distant sources, thereby achieving a high degree of rejection of background noise. Spatial selectivity is obtained through separating the different coils by a sufficient distance so that the source of interest primarily affects the pickup coil, closest to the source, and not the reference coils sensing the surrounding magnetic environment. Gradiometers are practically insensitive to uniform fields such as the large field of the earth. However, this selectivity is achieved at some cost in the overall sensitivity.

In a superconductive gradiometer the flux transporter and SQUID are mounted in a superinsulated dewar filled with liquid helium, keeping the sensing apparatus near 4 degrees Kelvin. The dewar (about 1.2 m in length) is generally mounted on a non-metallic support structure that allows its precise positioning over specific points on the subject's scalp (see Figure 3). These large single-channel sensors may before long be replaced by smaller multichannel devices refrigerated by cryocoolers reducing the need for liquid helium and large dewars.

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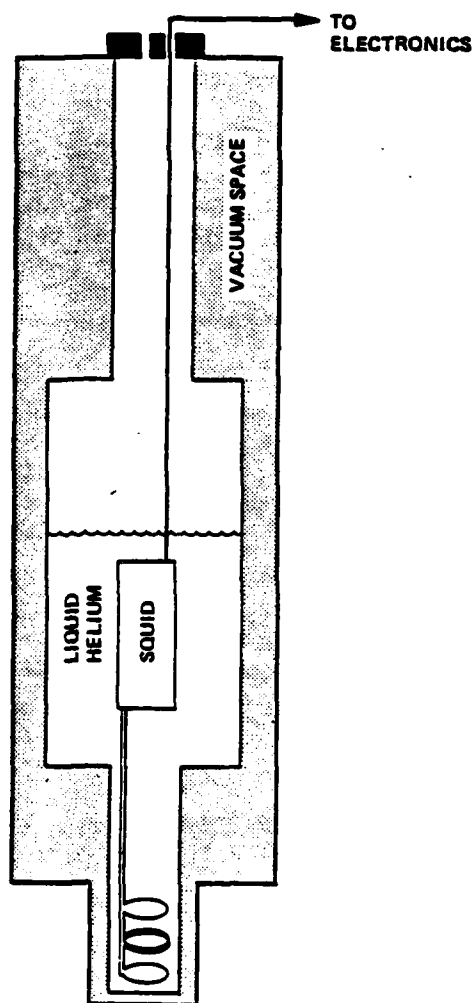


Figure 3. Superconductive magnetic sensor. The superinsulated dewar contains liquid helium which surrounds the SQUID amplifier and the sensing coils here configured as a second-derivative gradiometer.

5.1 NEUROMAGNETIC MAPPING.

The commercially available magnetic recording systems utilize a single-channel sensor that is coupled to a gradiometer configured to record the component of the field that is normal to the head. The output of the SQUID control circuitry is directly proportional to the gradient of magnetic flux and may be amplified and filtered with the same system used to perform EEG measurements. This serves to equalize phase shifts due to the analog filters and facilitates direct MEG-EEG comparisons.

In a typical recording session, the gradiometer is sequentially positioned through a matrix of closely spaced points thought to encompass the entire extracranial magnetic field produced by a given neural event. This matrix of points is generally referenced to skull landmarks such as lines separating the International 10-20 recording system (Jasper, 1958), or the orbitomeatal axis which is used in computerized tomography atlases (e.g., Matsui & Hirano, 1978).

Special precautions should be taken in MEG recording to eliminate the presence of artifacts due to the vibration of the sensor or to the stimulation equipment. Vibration artifacts are generally produced by unstable support of the dewar or subject or by the contact of the dewar with the hair or scalp of the subject. Stimulation artifacts can be minimized by the use of low-current devices placed at some distance from the sensor.

Brain magnetic fields may be related to an external event, such as sensory stimulation or voluntary motor activity, or may be produced spontaneously, as in the study of epileptiform discharges. In either case, some form of signal averaging is typically performed, time-locked to a series of successive events. Averaging improves both the signal to noise ratio and the statistical reliability of the signal. The amplitude of the time series at a particular latency is proportional to the instantaneous magnetic flux density at the recording point. The polarity of the time series represents the direction of the field lines at that point, either entering the head or emerging from the head.

The recordings from each point in the matrix may later be reassembled by computer into topographical maps representing the spatial distribution of the amplitude and polarity of the magnetic fields at selected points in time (Lehmann, 1977). A magnetic field map of an area on the scalp is considered complete when it reliably displays symmetrical field extrema of opposite polarity where the flux emerges from and reenters the head and when the strength of the field approaches zero at all borders of the map.

Localization of the source producing a particular magnetic field pattern depends both upon the measured properties of the field and upon the model assumed for the generating source. If the current dipole model is used, the orientation of the underlying source may be determined to be orthogonal to a line connecting the two field extrema. The surface location of the source is exactly midway between the extrema. The direction of the current may be determined by applying the right hand rule to the direction of field circulation.

Finally, the depth of the source may be calculated from the distance between the extrema and by making certain assumptions about the volume containing the source. The field pattern produced by a current dipole embedded in a finite conducting volume depends on the geometry of the volume. Cuffin and Cohen (1977) have summarized the derived patterns for the semi-infinite volume, the sphere and other shapes approximating that of the human cranium. In the case of the spherical approximation of the head, Williamson & Kaufman (1981a) have provided an algorithm to estimate the depth of sources. This algorithm depends on the diameter of the head at the surface location of the source and the length of the arc separating the two magnetic extrema obtained at the surface. The model of the current dipole in a conducting sphere has generally produced depth estimates that are consistent with general neuroanatomical data about the most likely locations of individual sources in the cortex (e.g., Richer, Barth, & Beatty, 1983; Romani, Williamson, & Kaufman, 1982.). It also should be noted that concentric variations in conductivity in a sphere, such as the skull, do not affect the pattern of the external magnetic field (Grynspan & Geselowitz, 1973). However, any serious deviations from the spherical model may affect the localization derived from the observed field pattern.

6.0 EVENT-RELATED FIELDS: THE VISUAL SYSTEM.

The magnetic response of cortical systems to stimulation or overt behavior has a waveshape that is similar to the event-related potential (ERP), consisting of components of differing amplitude and polarity. We have termed this magnetic response the event-related field (ERF). The neuromagnetic response of visual cortex was first described using steady-state ERFs to rapid stimulation (Brenner, Okada, MacIin, Williamson, & Kaufman, 1980; Brenner, Williamson, & Kaufman, 1975). For a 13 Hz flicker rate, the equivalent dipolar source of the response is located in the occipital cortex and oriented on a medial-to-lateral axis, perpendicular to the middle sagittal fissure.

The transient visual ERF to patterned stimulation contains a biphasic response corresponding in latency to the N100-P200 complex of the ERP. This response is restricted to occipital derivations on the cortex and reverse polarity from dorsal to ventral locations on the scalp in the region of Oz (Barth, Richer, & Beatty, 1982; Richer, Barth, & Beatty, 1983). This distribution is congruent with a current dipole oriented in a general medial-to-lateral axis (see Figure 4). Other studies have found earlier responses in generally posterior derivations of the scalp using unpatterned light flashes (Teyler, Cuffin, & Cohen, 1975; Zimmerman, Edrich, Zimmerman, & Riete, 1978).

The source of the visual ERF to left hemifield stimulation is generally located to the right of that to right hemifield stimulation (Brenner et al., 1981; Richer et al., 1983). Both sources are however very close to midline and the estimates of their depth below the scalp range between 12 and 25 mm. indicate that their most likely origin is in Brodmann's area 17. One study has found sources of increasing depth in the cortex with increases in the

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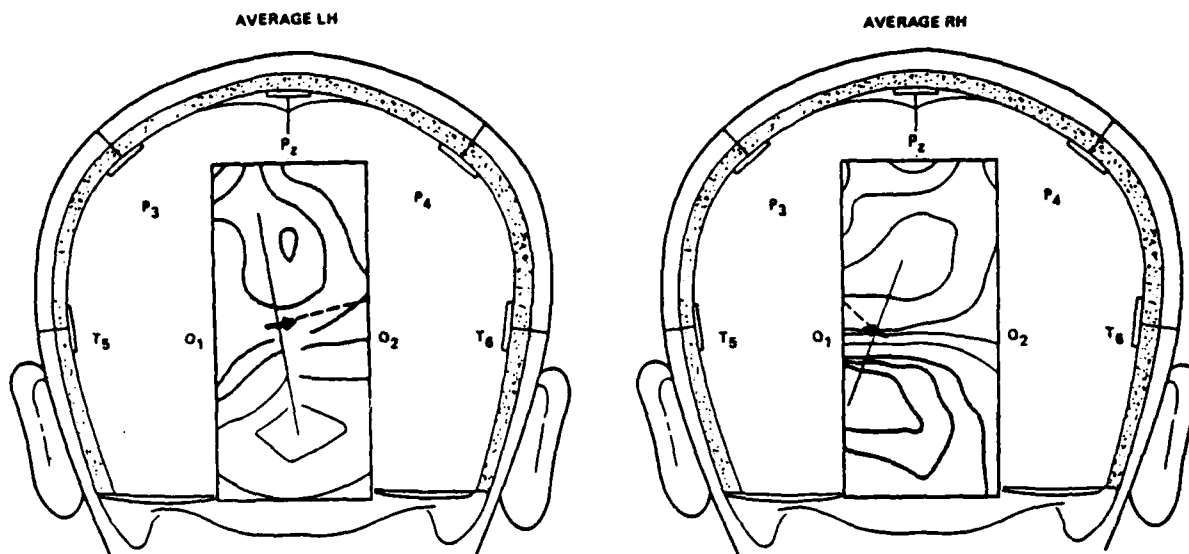


Figure 4. Magnetic field distributions of the 120 msec component of the ERF evoked by patterned visual stimulation in both the left hemifield (LH) and right hemifield (RH). These maps are from the averaged data of four subjects and cover 21 recording points spaced 2 cm apart. Stipled areas are those in which the field leaves the head, whereas solid areas are those in which the field enters the head. (Adapted from Richer, Barth & Beatty, in press).

retinal eccentricity of visual stimulation (MacLin, Okada, Kaufman, & Williamson, 1983). This arrangement corresponds with what is known of the retinotopic organization of area 17.

7.0 EVENT-RELATED FIELDS: THE AUDITORY SYSTEM.

The transient auditory evoked field also contains a biphasic response with peaks at about 100 msec and 180 msec (Elberling, Bak, Kofoed, Lebech, & Saermark, 1980; Hari, Aittoniemi, Jarvinen, Katila, & Varpula, 1980; Reite, Edrich, Zimmerman, & Zimmerman, 1978; Zimmerman, Reite, & Zimmerman, 1981). Its source has been localized in the superior temporal region and its main orientation is along the ventro-superior axis, possibly normal to the sylvian fissure.

The ERF to clicks was found to be of lower amplitude than that to tones of the same intensity (Reite, Zimmerman, & Zimmerman, 1982). Since this effect is not seen in the ERP, this observation may point to a difference in the intracellular current density of cortical sources for click and tone stimuli.

The auditory response to both tones and clicks is larger to contralateral than to ipsilateral stimulation (Elberling, Bak, Kofoed, Lebech, & Saermark, 1982b; Reite, Zimmerman, & Zimmerman, 1981). The asymmetry between the response of each hemisphere is most pronounced in the case of right ear stimulation, for which the left hemisphere response is much larger than the right hemisphere response (see Figure 5). Elberling et al., (1981) also report that contralateral ERF responses occur about 9 msec earlier than corresponding ipsilateral responses.

These laterality effects contrast with the widespread nature of the ERP to unilateral stimulation. This is partly due to the fact that the ERF measures a restricted source in the superior temporal cortex of a single hemisphere whereas the ERP is probably affected by multiple bilateral sources.

There have been reports of systematic differences in the scalp distribution of the ERF to tones of different frequencies (Elberling, Bak, Kofoed, Lebech, & Saermark, 1982a; Romani, Williamson, & Kaufman, 1982a). This suggests a tonotopic organization of the auditory cortex. However, there are still questions concerning the relative arrangement of the sources responsible for different tone frequencies. Sources active for different frequencies could differ in their location on the anterior-posterior axis, in their depth in the sylvian fissure or in the size of the active cortical area.

Many investigations have addressed the question of the relationship between the biphasic ERF and the vertex N100-P200 complex of the auditory ERP. The auditory ERF is affected by the inter-stimulus interval in a manner similar to the N100-P200 (Johnson, Richer, & Beatty, Note 1; Tuomisto, Hari, Katila, Poutanen, & Varpula, 1982), although the ERF seems

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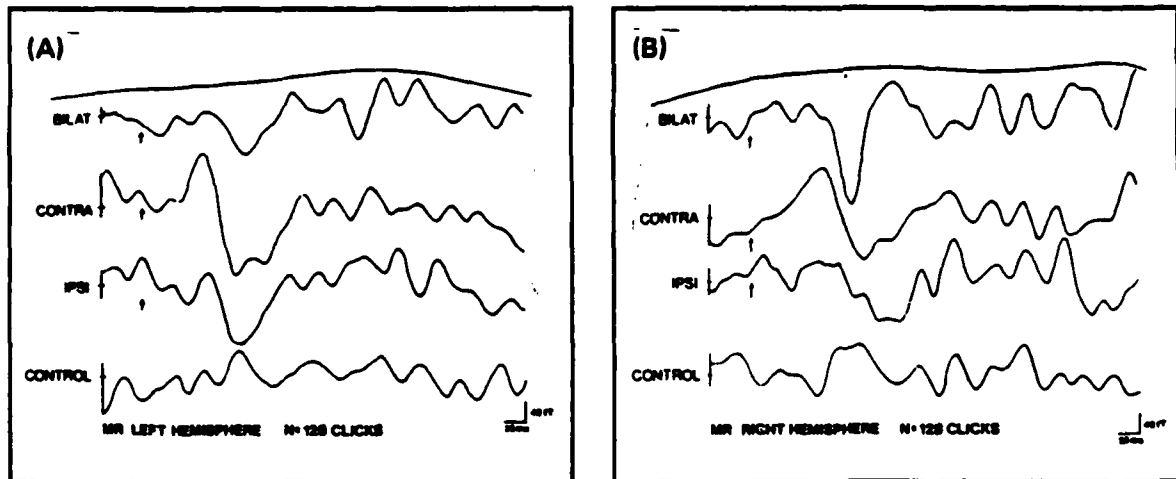


Figure 5. Auditory evoked fields from contralateral, ipsilateral, and bilateral phasic stimulation of (A) left and (B) right hemispheres. Notice the more pronounced laterality effect in the left hemisphere. (From Reite, Zimmerman, & Zimmerman, 1981).

to plateau earlier than the ERP for very long intervals. The effect of intensity on the two responses seems to be dissociated at levels higher than 60 dB (Reite, Zimmerman, Edrich, & Zimmerman, 1982). ERF amplitude saturates at about 60 dB, whereas the ERP increases almost linearly at higher intensities. The plateau in the amplitude of the ERF is accompanied by a plateau in the inverse function relating peak latency to intensity (Elberling et al., 1981). These data confirm that the auditory ERF is indexing a more restricted activity than the ERP. This concept is in agreement with suggestions that the N100-P200 complex of the ERP has multiple sources (Picton, Woods, Stuss, & Campbell, 1978).

8.0 EVENT-RELATED FIELDS: THE SOMATOSENSORY SYSTEM.

The cortical magnetic response to somatic stimulation has been localized to central regions of the head in both transient and steady-state ERFs. (Brenner, Lipton, Kaufman, & Williamson, 1978; Okada, Kaufman, Brenner, & Williamson, 1981). The responses obtained to hand and wrist stimulation are restricted to the hemisphere contralateral to the side that is stimulated and the sources underlying them are oriented in a general anterior-posterior axis, most probably perpendicular to the Rolandic fissure. The sources for different body parts are arranged topographically, being more ventral for the thumb than for the little finger (Brenner et al., 1978) and more dorsal for peroneal than median nerve stimulation (Teszner, Hari, & Nicolas, 1983; see Figure 6).

The transient somatosensory ERF is composed of at least four components. The biphasic response between 80 and 250 msec is analogous to the somatosensory N100-P200. This complex is preceded by components peaking at 25 and 45 msec (Okada et al., 1981). The early response bears a close relationship to the evoked potential recorded from the pial surface with median nerve stimulation (Goff, Williamson, Van Gilder, Allison, & Fisher, 1980). The pial ERP reverses polarity across the central sulcus in an axis that is perpendicular to the magnetic axis of polarity reversal. This result would be expected if the same discrete current source perpendicular to the sulcus was generating both electrical and magnetic fields. Thus, for simple superficial sources, the precision of the MEG can parallel that of invasive pial measurements.

9.0 EVENT-RELATED FIELDS: THE MOTOR SYSTEM.

ERFs have also been observed in relation to the initiation of simple ballistic movements (Deecke, Weinberg, & Brickett, 1982; Hari, Antervo, Katila, Poutanen, Sapanen, Tuomisto, & Varpula, 1982; Okada, Williamson, & Kaufman, 1982; Richer, Johnson, & Beatty, 1982; Weinberg, Deecke, Brickett, & Boschert, 1983). A slow component of the ERF preceding EMG onset by more than one second has been found to reverse polarity from frontal to parietal locations. This component corresponds in latency to the

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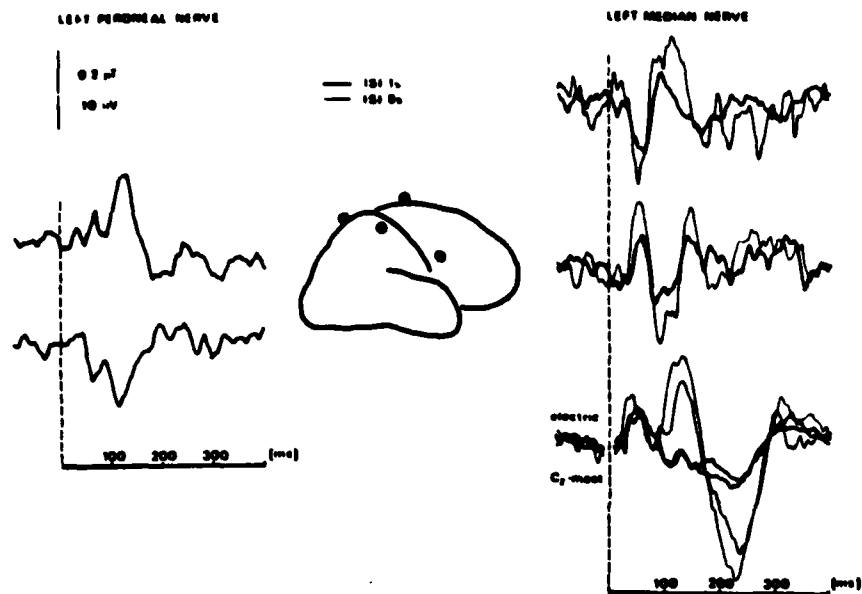


Figure 6. Polarity reversals in the magnetic fields evoked by left peroneal and median nerve stimulation. The peroneal source is located more dorsally than the median nerve source. (From Tetzner, Hari, & Nicolas, in press).

readiness potential of the ERP (Kornhuber & Deecke, 1964).

A more transient component peaking around EMG onset reverses polarity from superior to ventral locations in central regions of the scalp and its source is oriented frontally. This would be expected if the source of this motor field was in the dentritic fields of the frontal wall of the Rolandic fissure. There is a close agreement between the location of the cortical source of the ERF to finger stimulation and that obtained for the transient motor ERF to finger flexions (Richer et al., 1982; see Figure 7). This component appears to correspond to the motor potential of the ERP.

10.0 EVENT-RELATED FIELDS: COGNITIVE PROCESSING.

It has long been known that the ERP contains late components related to task-relevant processing of stimuli and not to the physical characteristics of stimuli. The localization power of the MEG can thus be expected to provide some much needed insights into the neurophysiology underlying these processes. In addition to the neuroanatomical information, the MEG should theoretically provide the possibility to dissociate temporally overlapping sources originating in different locations. This task has however only been undertaken recently and answers about the origin of specific cognitive electrophysiological components are only preliminary at this time.

A central issue in the electrophysiology of cognitive processing concerns P300, a late component in the ERP, first reported in 1965 (Sutton, Braren, Zubin, & John, 1965). The P300 is a positive component occurring from 280 to 500 msec post-stimulus that is elicited by rare task-relevant stimuli in discrimination or classification tasks. On the scalp, the electrical P300 generally has a diffuse bilateral distribution maximal at midline centroparietal locations (Donchin, 1979).

Richer, Johnson, and Beatty (Note 2) have recorded late components of the ERF similar in latency to the electrical P300 complex. Subjects listened to sequences of tones in which tones differing in frequency from the standard tones were randomly interspersed with a probability of .2. The late magnetic component (M300) was not present in ERFs to frequent tones and was not present when only one type of tone was presented and no discrimination was necessary. M300 also appeared when the omission of a tone was the rare event to be discriminated and it also varied in amplitude with the probability of the rare stimulus. These effects are all characteristic of the P300 recorded electrically.

As can be seen in Figure 8, the auditory M300 appears to originate in superior temporal cortex in close vicinity to the origin of auditory evoked responses in each hemisphere; it is oriented in a general ventro-dorsal axis. The source was located more frontally in the right hemisphere compared to the left hemisphere. This trend agrees with data obtained on the sensory response of auditory cortex with both the MEG and positron-emission tomography data (Elberling et al., 1982b; Mazziotta et al., 1982).

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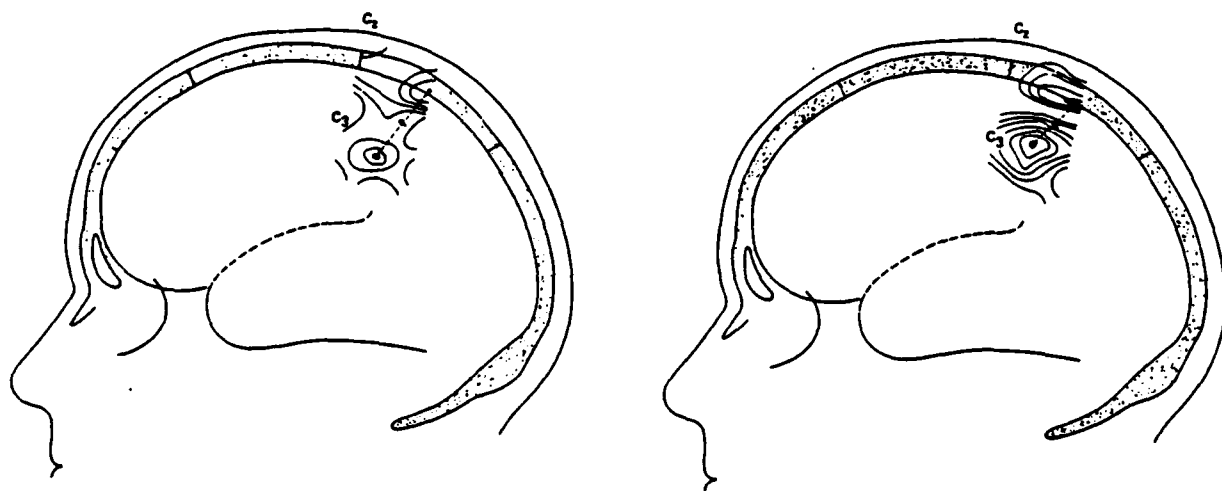


Figure 7. Magnetic field distributions for the 120 msec component of somatosensory response to electrical stimulation of the right index finger (right panel) and the phasic pre-motor component accompanying right index flexions (left panel). Arrows indicate equivalent dipole location under the spherical model. The two sources originate in very similar locations in central cortex and have opposite directions.

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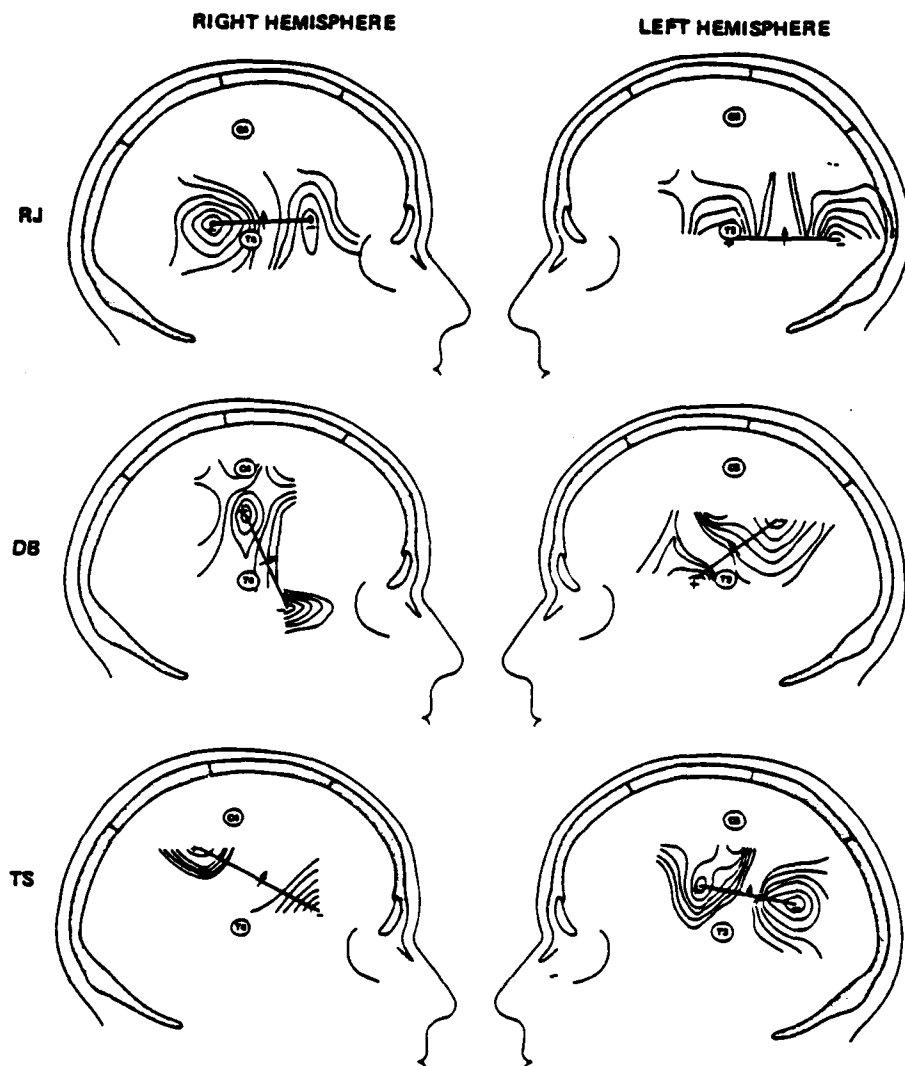


Figure 8. Distribution of the late auditory discrimination component of the event-related field in three subjects. All sources were estimated to be in temporal neocortex not deeper than 4 cm below the scalp and in cortex adjacent to the origin of the sensory auditory evoked response.

Richer, Johnson, and Beatty (Note 3) also found preliminary evidence for a visual M300 evoked during pattern discrimination. The source seems to be located in the vicinity of the parieto-occipital junction and is oriented posteriorly in each hemisphere. These data suggest that P300 is not a general non-specific process as was believed (e.g. Pritchard, 1981), but reflects modality-specific cognitive activity. The magnetic response may not reflect all the components of the electrical P300 but this wave appears to contain a large component originating in sensory-specific (possibly association) cortex.

Okada, Kaufman, and Williamson (1983) have recorded magnetic activity around 450 msec post-stimulus which tended to be larger in ERFs to rare visual stimuli compared to those of frequent stimuli. They believe that the source responsible for the field distribution of that component is in the limbic system.

One study also reported the existence of a magnetic counterpart to the contingent negative variation in forewarned reactions (Weinberg et al., 1982). A rolandic location of the generators has been tentatively suggested for the early component of this slow response, but the source has not been clearly localized as yet.

11.0 CLINICAL MAGNETOENCEPHALOGRAPHY.

The same properties of neuromagnetic recording that permit the localization of current sources within the normal brain may be applied usefully to the study of selected forms of brain pathology. Although clinical neuromagnetometry is still in its infancy, the initial results are encouraging.

The earliest recording of abnormal activity in the human brain was reported by Cohen (1972). A single patient with psychomotor (complex partial) seizures was studied. During hyperventilation, the patient displayed slow delta activity in both the raw EEG and MEG. The EEG also showed prominent activity in the theta frequency band although this was not evident in the MEG, reflecting a partial dissociation between the recordable signal of the EEG and the MEG.

The dissociation between EEG and MEG was also noted in a clinical investigation performed several years later at the same MIT laboratory by Hughes, Cohen, Mayman, Scholl, and Hendrix (1977). Neuromagnetic measurements were taken from a total of ten patients with a variety of neurological disorders, including brain tumor, petit mal epilepsy, diffuse abnormalities, and several psychiatric disorders accompanied by prominent slow (delta) waves. In patients where delta activity could be measured in the EEG, an inconsistent appearance of this activity was found in the MEG measured from a number of scalp locations. In the case of 3/sec spike and wave complexes accompanying petit mal absence, the wave was greatly attenuated in the MEG whereas the spike was easily recorded. These results might reflect separate current dipoles of differing orientation.

Recently, Modena, Ricci, Barbanera, Leoni, Romani and Carelli (1982) have investigated the MEG signals produced by specific categories of seizure disorder. Magnetic fields associated with the 3/sec spike and wave complex of petit mal absence show a great deal of variability both among subjects and among different scalp locations recorded within the same subject. Modena et al. report that the relative amplitude of the spike with respect to the wave changes over brain regions, suggesting separate generators for the two components that differ not so much in orientation as in spatial location or configuration.

Modena et al. also measured magnetic fields produced by paroxysmal interictal activity in a series of patients with focal seizure disorders. The largest correspondence between the EEG and MEG signals was found in cases where the epileptic focus was superficial, on the outer cortex. Basal and medial foci produced little or no measureable MEG activity. Although no attempt was made to spatially map the interictal magnetic activity, Modena and his colleagues noted that small changes in scalp location could greatly affect its amplitude.

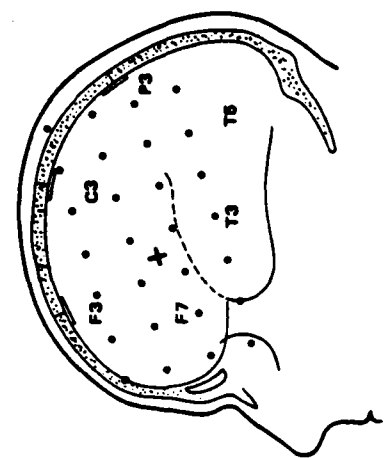
Neuromagnetic measurements may make their greatest clinical contribution in the investigation of focal (partial) seizure disorders, since localizing information of primary importance in such cases. The interictal spike characterizing complex partial seizure disorders provide a clear signal of focal origin. Localization of epileptiform current sources is obtained by systematically mapping a series of scalp locations covering points where the field maximally emerges from and reenters the cranium. Averaging is accomplished by using the interictal spike in the EEG as the temporal reference point. An averaged magnetic spike may be computed for each of a series of scalp locations covering the region of the epileptic focus. The magnetic field pattern for each of the components of the spike complex may then be reconstructed and the location of underlying sources determined.

This technique has been successfully applied to a number of patients with complex partial seizure disorders (Barth, Sutherling, Engel, and Beatty, 1982; Barth, Sutherling, Beatty, and Engel, 1982; Sutherling, Barth, Engel, and Beatty, 1983). Figure 9 displays an example of a magnetic spike complex recorded from a child with right temporo-frontal (Sylvian) spike discharges. In this subject, a dependent contralateral homologous EEG spike focus was also recorded. Averaged magnetic spikes for each of the points within the MEG recording matrices display an orderly amplitude and polarity distribution. The magnetic field from the dependant spike focus in the left hemisphere follows that of the right by 20 msec., probably reflecting its dependence on transcallosal discharge. The morphology of the magnetic spike is very similar to that of the electrical spike averaged from the primary EEG focus. Field maps of the magnetic spike (M1) and sharp wave (M2) of the right hemisphere reveal a common source for these components in the right frontal operculum. Similar field maps localize a common source for the secondary discharge in an homologous region of the left hemisphere. Figure 10 presents the data of a second patient with an interictal spike focus located in the left anterior temporal lobe.

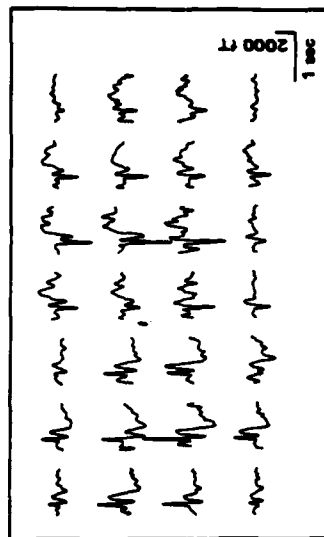
The spatial resolution of the spike-averaged MEG in certain cases

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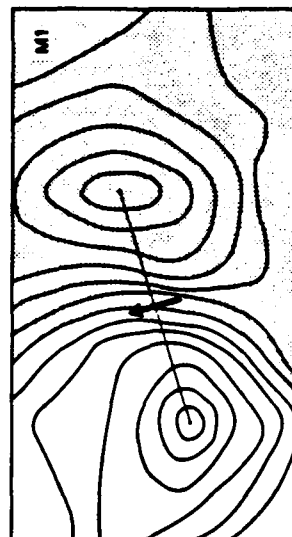
Figure 9. Averaged magnetic spike activity measured from the right and left hemispheres of a subject whose interictal spikes were produced by single sources in the bilateral opercular regions. (A and H) Rectangular MEG measurement matrices (2 cm spacing) oriented along the temporal axes of both hemispheres. Crosses mark the location of MEG spike foci. (B and I) Average magnetic spikes for each point within the right and left hemisphere MEG matrices. (E) Average EEG spike recorded from the T4-T6 derivation over the right hemisphere (90 microvolts baseline to peak, T4 negative up; negative spike phase reversed at T4-F8). (F) Enlargement of two average traces near the extrema of the magnetic fields from the left (solid) and right (dotted) area of the right hemisphere MEG matrix, demonstrating two reliable temporal components (M1 and M2) and opposing polarity reflecting the magnetic field simultaneously leaving (up) and entering (down) the cortex. (G) Magnetic spike from the left hemisphere (dotted, rescaled for comparison) is delayed by 20 msec when compared to that of the right (solid). (C and D) Isocontour plots demonstrating the amplitude (750 fT. per bar) and polarity (light indicates emerging and shaded, reentering) distribution of magnetic fields associated with M1 and M2 of the right hemisphere. Straight lines connecting the field extrema demark the orientation of the magnetic fields. Arrows represent the location and polarity of underlying current sources. (J and K) Similar contour plots displaying magnetic field distributions of M1 and M2 over the left hemispheric focus.



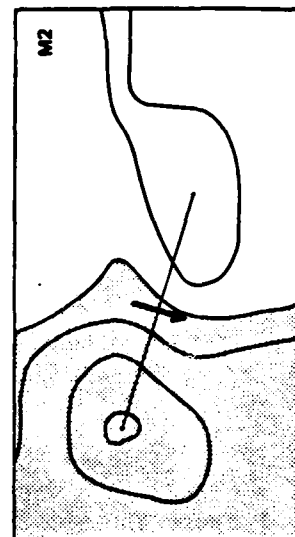
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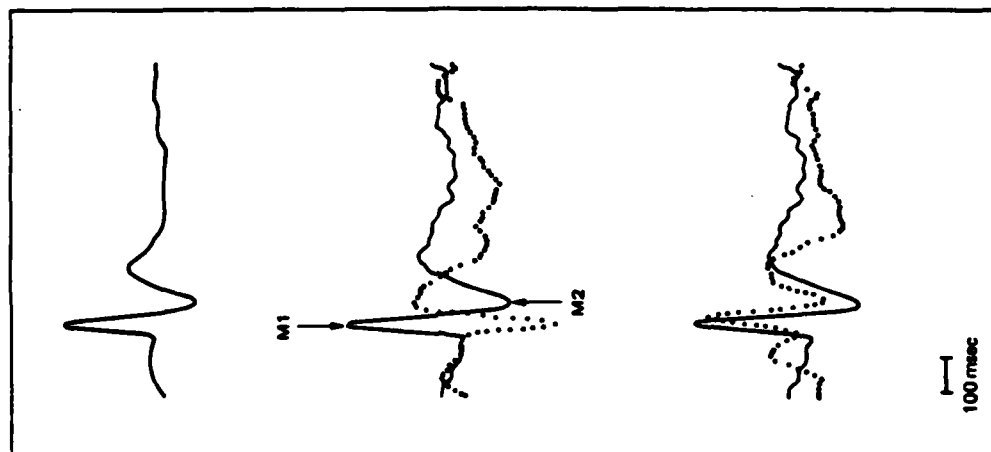
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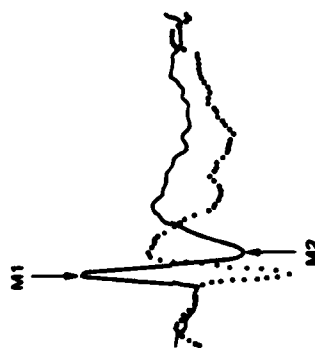
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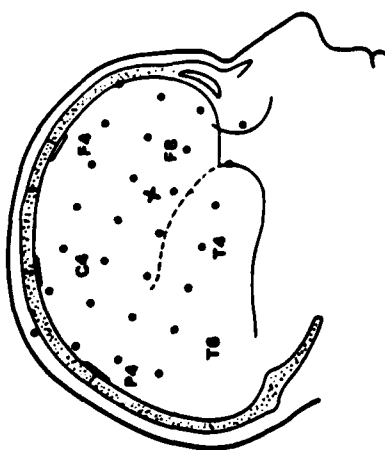
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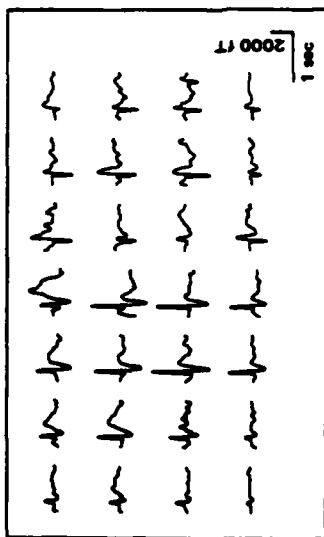
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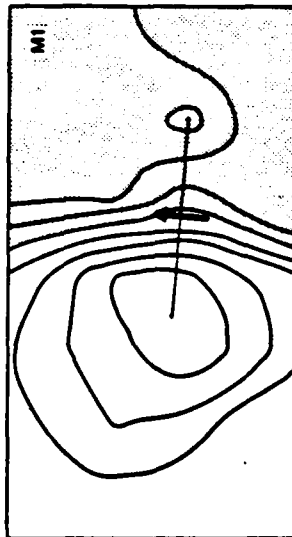
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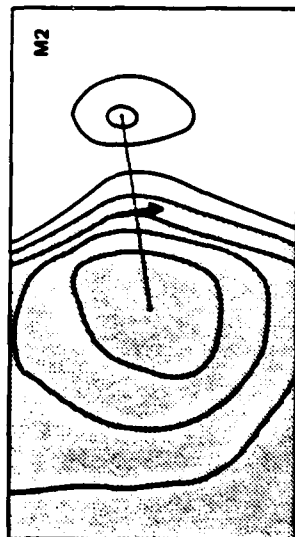
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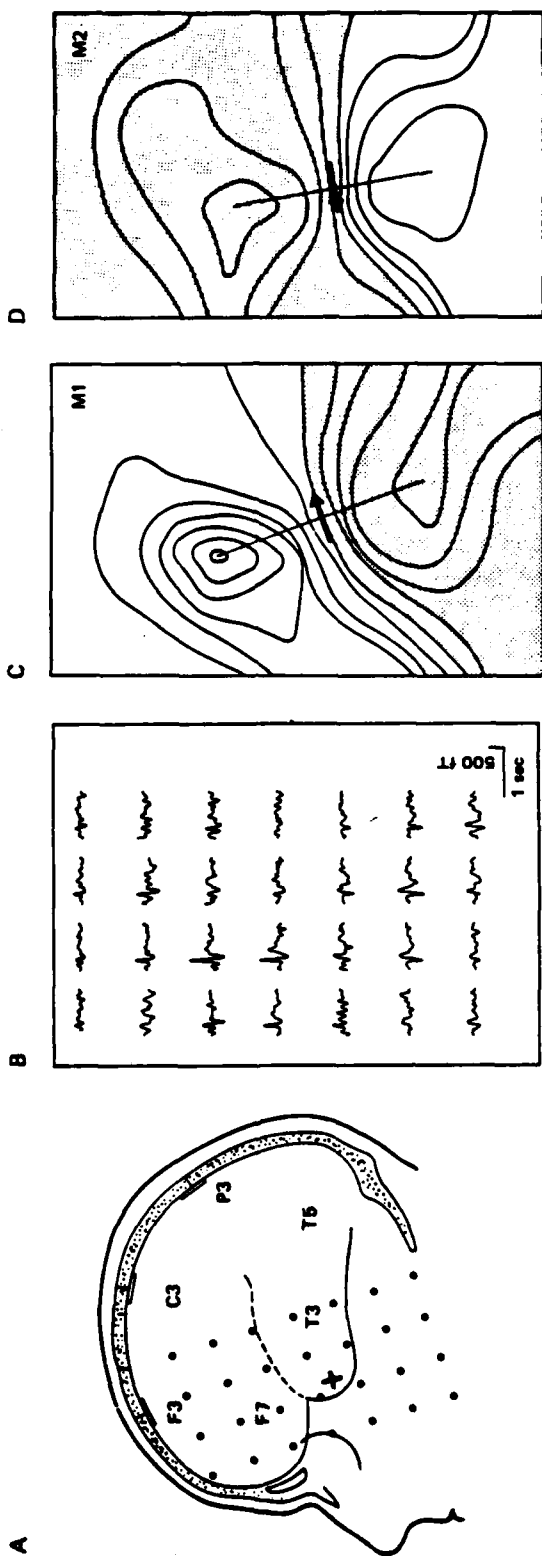
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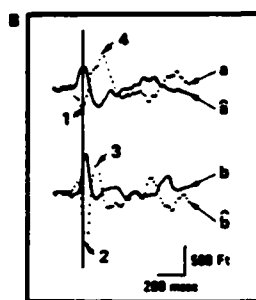
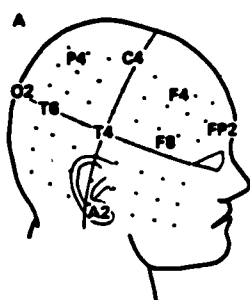
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Figure 10. Average magnetic spike activity from another subject whose interictal spike complex was produced by a single cortical source in the left anterior temporal lobe. (A) Rectangular MEG measurement matrix covering the left anterior temporal region. A cross marks the spot of the MEG spike focus. (B) Average magnetic spikes obtained from each point in the matrix. (C and D) Isocontour plots (similar to Figure 1) displaying the amplitude and polarity distributions of the generators of M1 and M2. The EEG spike was similar in morphology to the MEG spike and maximal at T1, below and posterior to F7.



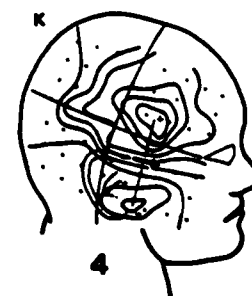
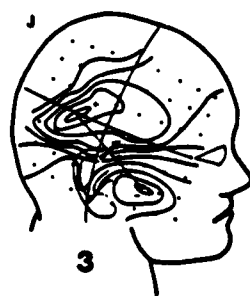
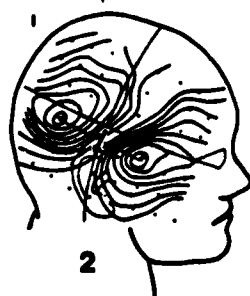
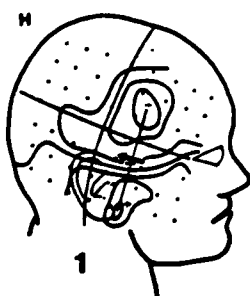
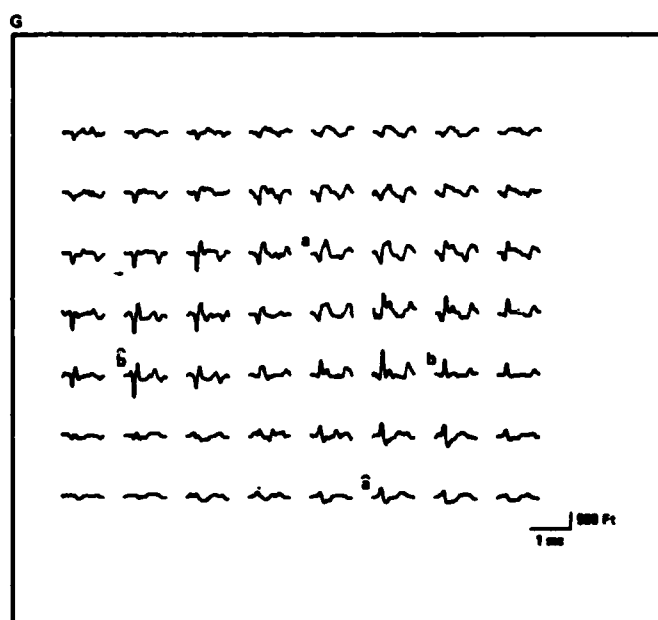
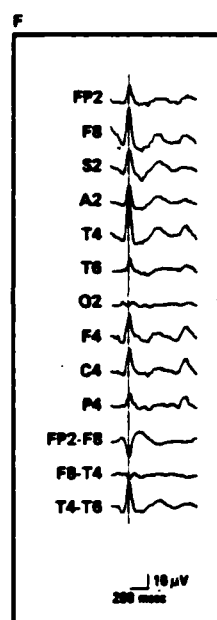
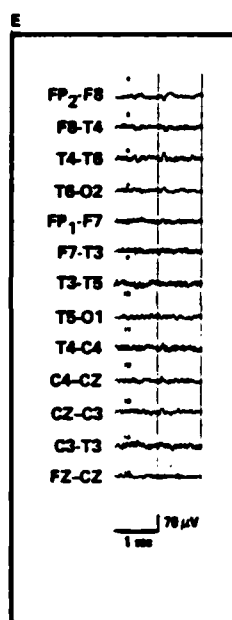
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Figure. 11. Averaged electrical and magnetic spike activity measured from the right hemisphere of a subject whose interictal spike complex was produced by multiple sources in the right mid-temporal lobe. (A) Rectangular MEG measurement matrix (2 cm spacing) oriented along the temporal axis. EEG electrodes are marked according to the International 10/20 System. The spenoidal electrode (S2) is not labeled. (B) Enlargements of averaged magnetic spikes from separate symmetrical regions ("a" and "b") of the scalp, demonstrating 4 temporal components (1, 2, 3 and 4) and the opposing polarity reflecting the magnetic field simultaneously emerging from (upward) and reentering (downward) the cranium. (C) and (D) CT scan sections at the levels of sources "a" and "b" respectively show the depth of the source (cross) located along a line connecting the surface location of the source marked with a washer (arrow) to the center of the cranium. (E) Spike in the raw EEG recorded from both hemispheres. (F) Averaged EEG spike from 3 bipolar channels (lower 3 traces) and 10 electrodes referenced to a non-cephalic site (upper 10 traces). Line indicates time reference point. (G) Averaged magnetic spikes recorded from each position of the MEG matrix with two distinct symmetrical regions of differing morphology marked "a" and "b". (H), (I), (J) and (K) Isocontour maps displaying the magnetic fields for each of the 4 temporal components of the magnetic spike complex (see text for details).



20 mm

20 mm



permits the localization of multiple current sources underlying interictal spiking within a single hemisphere. Sequential analysis of spatio-temporal discharge patterns frequently reveals the magnetic spike complex to be comprised of a primary source with activity preceding that of secondary dependent sources (Barth, Sutherling, Engel, & Beatty, Note 4). Figure 11 displays evidence of multiple sources producing interictal spiking in a patient with complex partial seizures. Here, a rather extensive measurement matrix was employed to completely encompass the magnetic field pattern, shown marked on an outline of the patients head. In the matrix of averaged magnetic spikes, two separate pairs of extrema can be discerned (a-a and b-b), differing in both morphology and timing. This suggests the presence of two distinct sources. Magnetic field maps constructed for each of the components of both sources demonstrate an orderly spatiotemporal discharge pattern. The lateral mid-temporal focus produces a primary discharge, followed by a biphasic response in the more posterior lateral temporal focus, and concludes with a discharge of opposite polarity, once again in the mid-temporal focus. The presence of multiple sources underlying interictal spiking is a more frequent finding than that of single sources.

In these and other cases where the epileptogenic focus is located near the surface of the cortex, three dimensional localization may be provided by neuromagnetic measures. However, deeper, more mesial interictal discharges may also be recorded. Although the present single channel systems are inadequate for localizing singular pathological events such as focal seizure onset, preliminary data indicates that the magnetic fields associated with focal seizures are of sufficient strength to be recorded extracranially without signal averaging. Further analysis of the orientation, polarity and timing of both interictal and ictal magnetic fields, coupled with histological data, may help resolve a number of issues concerning both patient treatment and the understanding of epileptic processes.

12.0 CONCLUSIONS.

Very often discoveries in the natural sciences have been the direct result of advances in the technological sciences that provide instruments of measurement. The recently developed capacity to sense the weak magnetic fields produced by the human brain is one such instance. Similar in many respects to electroencephalography, magnetoencephalography provides a unique perspective as to the locus of synchronous synaptic activity within the large neurons of the brain. Many events that have been recorded previously by electroencephalographic methods have been recorded and localized magnetoencephalographically.

Neuromagnetic sensors, based upon superconductive quantum interference devices, record the exit and entry of magnetic fields from the head. From such field measurements, the position, orientation, and depth of the generating dipole current sources may be modelled. When coupled with other knowledge concerning the anatomy and physiology of brain, empirically obtained field maps have been remarkably revealing.

The major contribution of neuromagnetometry to the study of event-related fields has been the localization of the sources of brain activity in different cortical systems. To date, anatomically plausible localizations have been obtained for the sources of magnetic fields elicited by visual, auditory, and somatosensory stimuli, as well as for magnetic activity related to movement initiation. Neuromagnetic measurement has permitted the study of the topographic organization of all three perceptual systems and the interhemispheric differences in the responses of these systems. The ERF has also been used to clarify the neuroanatomical basis of electrical measures and to separate temporally overlapping components of the ERP. Further, the ERF is starting to delineate sources of activity related to discrimination and other cognitive processes and we can expect it to be very helpful in the study of the interaction of multiple cortical systems in human performance.

Although neuromagnetometry has been applied only recently in clinical investigations, the initial results have been quite promising. The electrical disturbances produced by a variety of seizure disorders, including both ictal as well as interictal activity, have been shown to produce detectable extracranial magnetic fields. In the case of partial seizure disorders, neuromagnetic measurements have permitted the localization of discrete sources underlying the interictal spike. Analysis of spatiotemporal discharge patterns in many instances shows evidence of multiple, interrelated sources producing interictal spike complexes.

Magnetoencephalography has introduced a new and productive phase in the study of the gross electrical signals of the brain. It has provided an initial localization of the sources of many brain signals that have been of uncertain origin. Thus, magnetoencephalography complements electroencephalography; properly used, the MEG can tell where the more easily recordable EEG signals probably originate. In this way, neuromagnetic recording helps one to understand the ways in which brain electrical activity reflects brain anatomy and physiology.

13.0 FURTHER READING.

A number of excellent reviews of various aspects of neuromagnetic recording are now available. Williamson and Kaufman have provided both a detailed overview of a wide range of biomagnetic phenomena (Williamson and Kaufman, 1981b) as well as a review of brain magnetic activity (Williamson and Kaufman, 1981a). Reite and Zimmerman (1978) have written a comprehensive review of the early literature on brain magnetic activity. Issues concerning instrumentation are treated by Romani, Williamson, and Kaufman (1982b) and by Katila (1981).

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FOOTNOTE

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